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Figure 1 A, B, and C

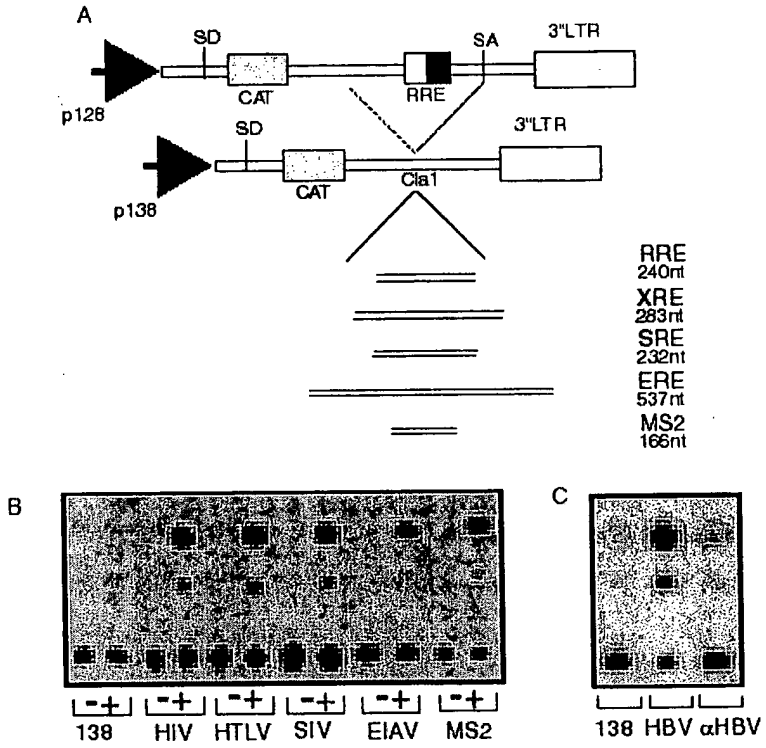


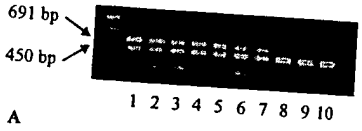
Figure 2

```
HTLV : 1 MPKTRRRPRRSQRKRPPTPW------PTSQGLDRVFFSDTQSTCLETVYKATGAPSLGD 53
       RNA binding domain and NLS
 BLV : 1 MPKERRSRRRPQ---PIIRWQVLLVGGPTLYMPARPWFCPMMSPSMP-----GAPSAGP 51

HTLV :54 YVRPAYIVTPYWPPVQSIRSPGTPSMDALSAQLYSSLSLD--SPPSPPREPLRPSRSLP-RQ 112
                                          NES
 BLV : 52 MSDSNSKGSTPRSPARPTVSTGPP-MDDLAASMER-CSLDCMSPRPAPKGPDDSGSTAPFRP 111

HTLV: 113 SLIQPPTFH-PPSSRP-----CANTP 132
       Dominant Negative Mutation
 BLV : 112 FALSPARFHFPPSSGPPSSPTNANCP 137
```

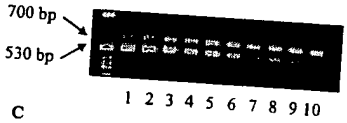
Figure 3

Figure 4

Figure 5 A, B, C, and D

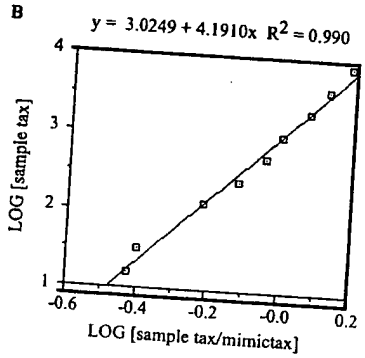


A



C

B



D

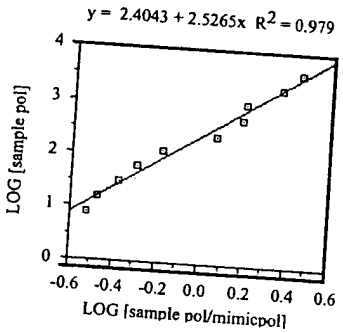


Figure 6

SEQ ID NO:1, Brex wild-type DNA Seqence

ATG CCT AAA AAA CGA CGG TCC CGA AGA CGC CCA CAA CCG ATC ATC AGA TGG CAA
GTG TTG TTG GTT GGG GGC CCC ACT CTC TAC ATG CCT GCC CGG CCC TGG TTT TGT
CCA ATG ATG TCA CCA TCG ATG CCT GGT GCC CCC TCT GCG GGC CCC ATG AGC GAC
TCC AAT TCG AAA GGA TCG ACA CCA CGC TCA CCT GCG AGA CCC ACC GTA TCA ACT
GGA CCG CCG ATG GAC GAC CTT GCG GCC TCA ATG GAA CGT TGT TCC CTC GAC TGC
ATG TCT CCG AGA CCC GCC CCC AAG GGC CCC GAC GAC TCT GGA TCA ACT GCC CCC
TTC CGG CCG TTC GCG CTC AGC CCG GCC CGG TTT CAC TTT CCC CCT TCG AGC GGT
CCC CCT TCC AGC CCT ACC AAT GCC AAT TGC CCT CGG CCT CTA GCG ACG GTT GCC
CCA TTA TCG GGC ACG GCC TTC TTC CCT GGA ACA ACT TAG

Figure 7

SEQ ID NO:2, Brex wild-type amino acid sequence

Met Pro Lys Lys Arg Arg Ser Arg Arg Arg Pro Gln Pro Ile Ile Arg Trp Gln
Val Leu Leu Val Gly Gly Pro Thr Leu Tyr Met Pro Ala Arg Pro Trp Phe Cys
Pro Met Met Ser Pro Ser Met Pro Gly Ala Pro Ser Ala Gly Pro Met Ser Asp
Ser Asn Ser Lys Gly Ser Thr Pro Arg Ser Pro Ala Arg Pro Thr Val Ser Thr
Gly Pro Pro Met Asp Asp Leu Ala Ala Ser Met Glu Arg Cys Ser Leu Asp Cys
Met Ser Pro Arg Pro Ala Pro Lys Gly Pro Asp Asp Ser Gly Ser Thr Ala Pro
Phe Arg Pro Phe Ala Leu Ser Pro Ala Arg Phe His Phe Pro Pro Ser Ser Gly
Pro Pro Ser Ser Pro Thr Asn Ala Asn Cys Pro Arg Pro Leu Ala Thr Val Ala
Pro Leu Ser Gly Thr Ala Phe Phe Pro Gly Thr Thr

Figure 8

SEQ ID NO:3, M7 DNA sequence

ATG CCT AAA AAA CGA CGG TCC CGA AGA CGC CCA CAA CCG ATC ATC AGA TGG CAA
GTG TTG TTG GTT GGG GGC CCC ACT CTC TAC ATG CCT GCC CGG CCC aga tct TGT
CCA ATG ATG TCA CCA TCG ATG CCT GGT GCC CCC TCT GCG GGC CCC ATG AGC GAC
TCC AAT TCG AAA GGA TCG ACA CCA CGC TCA CCT GCG AGA CCC ACC GTA TCA ACT
GGA CCG CCG ATG GAC GAC CTT GCG GCC TCA ATG GAA CGT TGT TCC CTC GAC TGC
ATG TCT CCG AGA CCC GCC CCC AAG GGC CCC GAC GAC TCT GGA TCA ACT GCC CCC
TTC CGG CCG TTC GCG CTC AGC CCG GCC CGG TTT CAC TTT CCC CCT TCG AGC GGT
CCC CCT TCC AGC CCT ACC AAT GCC AAT TGC CCT CGG CCT CTA GCG ACG GTT GCC
CCA TTA TCG GGC ACG GCC TTC TTC CCT GGA ACA ACT TAG

Figure 9

SEQ ID NO:4, M8 DNA sequence

ATG CCT AAA AAA CGA CGG TCC CGA AGA CGC CCA CAA CCG ATC ATC AGA TGG CAA
GTG TTG TTG GTT GGG GGC CCC ACT CTC TAC ATG CCT GCC CGG CCC TGG TTT TGT
CCa gat ctG TCA CCA TCG ATG CCT GGT GCC CCC TCT GCG GGC CCC ATG AGC GAC
TCC AAT TCG AAA GGA TCG ACA CCA CGC TCA CCT GCG AGA CCC ACC GTA TCA ACT
GGA CCG CCG ATG GAC GAC CTT GCG GCC TCA ATG GAA CGT TGT TCC CTC GAC TGC
ATG TCT CCG AGA CCC GCC CCC AAG GGC CCC GAC GAC TCT GGA TCA ACT GCC CCC
TTC CGG CCG TTC GCG CTC AGC CCG GCC CGG TTT CAC TTT CCC CCT TCG AGC GGT
CCC CCT TCC AGC CCT ACC AAT GCC AAT TGC CCT CGG CCT CTA GCG ACG GTT GCC
CCA TTA TCG GGC ACG GCC TTC TTC CCT GGA ACA ACT TAG

Figure 10

SEQ ID NO:5, M4 DNA sequence

ATG CCT AAA AAA CGA CGG TCC CGA AGA CGC CCA CAA CCG ATC ATC AGA TGG CAA
GTG TTG TTG GTT GGG GGC CCC ACT CTC TAC ATG CCT GCC CGG CCC TGG TTT TGT
CCA ATG ATG TCA CCA TCG ATG CCT GGT GCC CCC TCT GCG GGC CCC ATG AGC GAC
TCC AAT TCG AAA GGA TCG ACA CCA CGC TCA CCT GCG AGA CCC ACC GTA TCA ACT
GGA CCG CCG ATG GAC GAC CTT GCG GCC TCA ATG GAA CGT TGT TCC CTC GAC TGC
ATG TCT CCG AGA CCC GCC CCC AAG GGC CCC GAC GAC TCT GGA TCA ACT GCC CCC
TTC CGG CCG TTC GCG CTC AGC CCG GCC CGG TTa gat ctT CCC CCT TCG AGC GGT
CCC CCT TCC AGC CCT ACC AAT GCC AAT TGC CCT CGG CCT CTA GCG ACG GTT GCC
CCA TTA TCG GGC ACG GCC TTC TTC CCT GGA ACA ACT TAG

Figure 11

SEQ ID NO:6, M4Δ7 DNA sequence

ATG CCT AAA AAA CGA CGG TCC CGA AGA CGC CCA CAA CCG ATC ATC AGA TGG CAA
GTG TTG TTG GTT GGG GGC CCC ACT CTC TAC ATG CCT GCC CGG CCC AGA TCT GTC
ACC ATC GAT GCC TGG TGC CCC CTC TGC GGG CCC CAT GAG CGA CTC CAA TTC GAA
AGG ATC GAC ACC ACG CTC ACC TGC GAG ACC CAC CGT ATC AAC TGG ACC GCC GAT
GGA CGA CCT TGC GGC CTC AAT GGA ACG TTG TTC CCT CGA CTG CAT GTC TCC GAG
ACC CGC CCC CAA GGG CCC CGA CGA CTC TGG ATC AAC TGC CCC CTT CCG GCC GTT
CGC GCT CAG CCC GGC CCG GTT AGATCT TCC CCC TTC GAG CGG TCC CCC TTC CAG
CCC TAC CAA TGC CAA TTG CCC TCG GCC TCT AGC GAC GGT TGC CCC ATT ATC GGG
CAC GGC CTT CTT CCC TGG AAC AAC TTA GTA ACG CAT CCT GTC CTC AGA AAA GTC
CTT ATA TTA AAT CAA ATG GGA CCT CGA GGG GGG GCC CGA ATT CCG GAT CTT TGT
GAA GGA ACC TTA CTT CTG TGG TGT GAC ATA ATT GGA CAA ACT ACC TAC AGA GAT
TTA AAG CTC TAA

Figure 12

Sequence and translation of M7Stop construct in the pRS expression plasmid

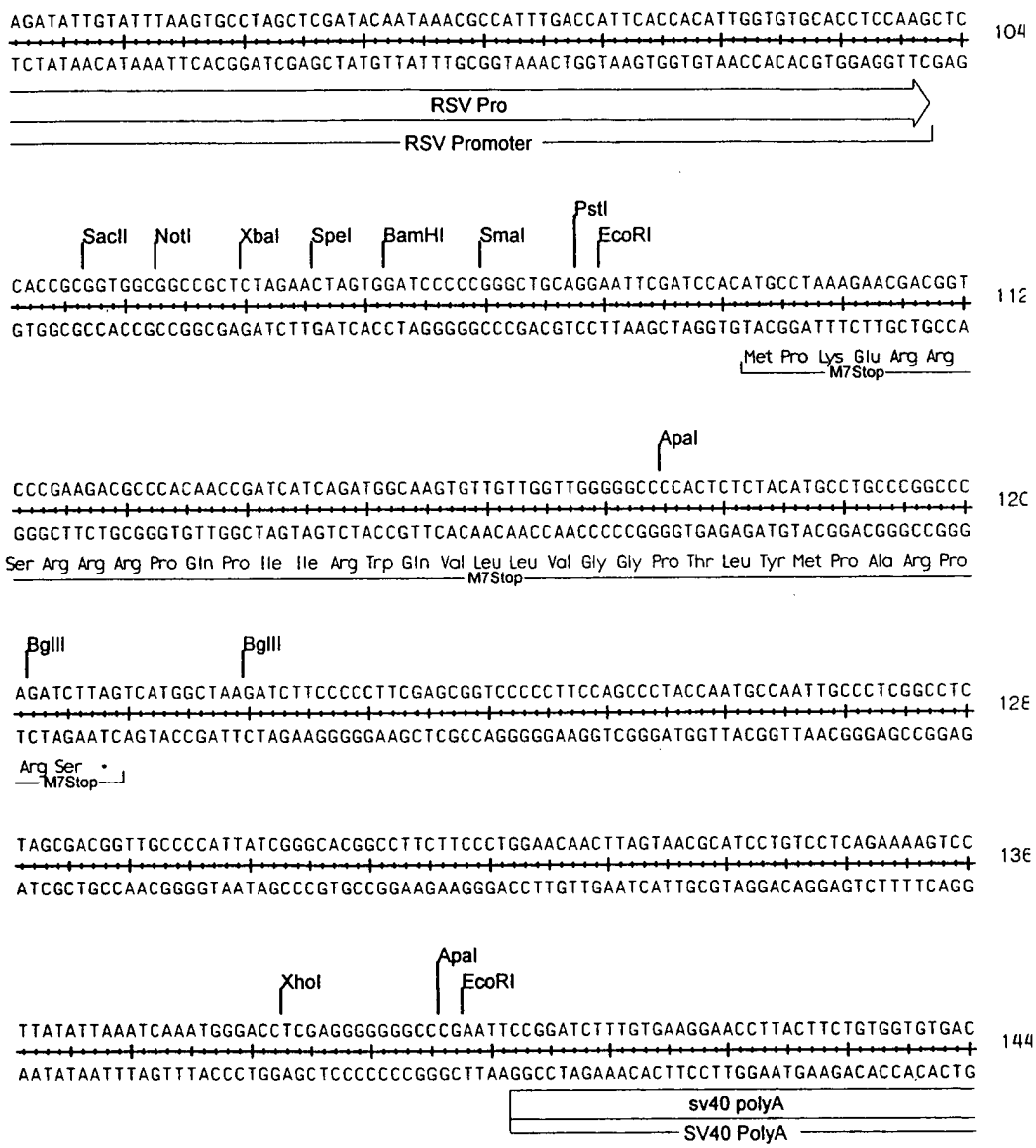


Figure 13

SEQ ID NO:8, M7 amino acid sequence

Met Pro Lys Lys Arg Arg Ser Arg Arg Arg Pro Gln Pro Ile Ile Arg Trp Gln
Val Leu Leu Val Gly Gly Pro Thr Leu Tyr Met Pro Ala Arg Pro Arg Ser Cys
Pro Met Met Ser Pro Ser Met Pro Gly Ala Pro Ser Ala Gly Pro Met Ser Asp
Ser Asn Ser Lys Gly Ser Thr Pro Arg Ser Pro Ala Arg Pro Thr Val Ser Thr
Gly Pro Pro Met Asp Asp Leu Ala Ala Ser Met Glu Arg Cys Ser Leu Asp Cys
Met Ser Pro Arg Pro Ala Pro Lys Gly Pro Asp Asp Ser Gly Ser Thr Ala Pro
Phe Arg Pro Phe Ala Leu Ser Pro Ala Arg Phe His Phe Pro Pro Ser Ser Gly
Pro Pro Ser Ser Pro Thr Asn Ala Asn Cys Pro Arg Pro Leu Ala Thr Val Ala
Pro Leu Ser Gly Thr Ala Phe Phe Pro Gly Thr Thr

Figure 14

SEQ ID NO:9, M8 amino acid sequence

Met Pro Lys Lys Arg Arg Ser Arg Arg Arg Pro Gln Pro Ile Ile Arg Trp Gln
Val Leu Leu Val Gly Gly Pro Thr Leu Tyr Met Pro Ala Arg Pro Trp Phe Cys
Pro Asp Leu Ser Pro Ser Met Pro Gly Ala Pro Ser Ala Gly Pro Met Ser Asp
Ser Asn Ser Lys Gly Ser Thr Pro Arg Ser Pro Ala Arg Pro Thr Val Ser Thr
Gly Pro Pro Met Asp Asp Leu Ala Ala Ser Met Glu Arg Cys Ser Leu Asp Cys
Met Ser Pro Arg Pro Ala Pro Lys Gly Pro Asp Asp Ser Gly Ser Thr Ala Pro
Phe Arg Pro Phe Ala Leu Ser Pro Ala Arg Phe His Phe Pro Pro Ser Ser Gly
Pro Pro Ser Ser Pro Thr Asn Ala Asn Cys Pro Arg Pro Leu Ala Thr Val Ala
Pro Leu Ser Gly Thr Ala Phe Phe Pro Gly Thr Thr

Figure 15

SEQ ID NO:10, M4 amino acid sequence

Met Pro Lys Lys Arg Arg Ser Arg Arg Arg Pro Gln Pro Ile Ile Arg Trp Gln
Val Leu Leu Val Gly Gly Pro Thr Leu Tyr Met Pro Ala Arg Pro Trp Phe Cys
Pro Met Met Ser Pro Ser Met Pro Gly Ala Pro Ser Ala Gly Pro Met Ser Asp
Ser Asn Ser Lys Gly Ser Thr Pro Arg Ser Pro Ala Arg Pro Thr Val Ser Thr
Gly Pro Pro Met Asp Asp Leu Ala Ala Ser Met Glu Arg Cys Ser Leu Asp Cys
Met Ser Pro Arg Pro Ala Pro Lys Gly Pro Asp Asp Ser Gly Ser Thr Ala Pro
Phe Arg Pro Phe Ala Leu Ser Pro Ala Arg Leu Asp Leu Pro Pro Ser Ser Gly
Pro Pro Ser Ser Pro Thr Asn Ala Asn Cys Pro Arg Pro Leu Ala Thr Val Ala
Pro Leu Ser Gly Thr Ala Phe Phe Pro Gly Thr Thr

Figure 16

SEQ ID NO:11, M4Δ7 amino acid sequence

Met Pro Lys Lys Arg Arg Ser Arg Arg Arg Pro Gln Pro Ile Ile Arg Trp Gln
Val Leu Leu Val Gly Gly Pro Thr Leu Tyr Met Pro Ala Arg Pro Arg Ser Val
Thr Ile Asp Ala Trp Cys Pro Leu Cys Gly Pro His Glu Arg Leu Gln Phe Glu
Arg Ile Asp Thr Thr Leu Thr Cys Glu Thr His Arg Ile Asn Trp Thr Ala Asp
Gly Arg Pro Cys Gly Leu Asn Gly Thr Leu Phe Pro Arg Leu His Val Ser Glu
Thr Arg Pro Gln Gly Pro Arg Arg Leu Trp Ile Asn Cys Pro Leu Pro Ala Val
Arg Ala Gln Pro Gly Pro Val Arg Ser Ser Pro Phe Glu Arg Ser Pro Phe Gln
Pro Tyr Gln Cys Gln Leu Pro Ser Ala Ser Ser Asp Gly Cys Pro Ile Ile Gly
His Gly Leu Leu Pro Trp Asn Asn Leu Val Thr His Pro Val Leu Arg Lys Val
Leu Ile Leu Asn Gln Met [redacted] Asp Leu Cys
Glu Gly Thr Leu Leu Leu Trp Cys Asp Ile Ile Gly Gln Thr Thr Tyr Arg Asp
Leu Lys Leu

Figure 17

HTLV: 113 SLIQPPTFH–PPSSRP-----CANTP 132

Dominant Negative Mutation

BLV : 112 FALSPARFHFPPSSGPPSSPTNANCP 137

M1 AAA

M2 DL

M3 DL

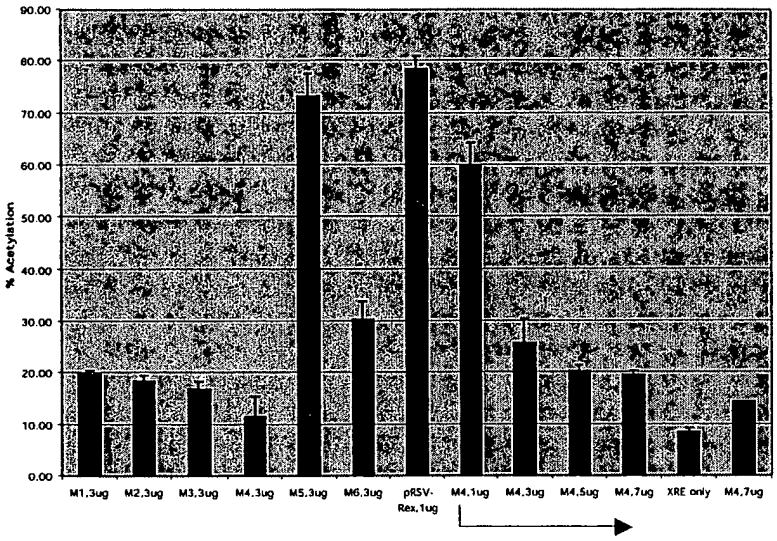
M4 DL

M5 DL

M6 (R85A) : Mutation of BLV NES

Figure 18 A and B

(A)



(B)

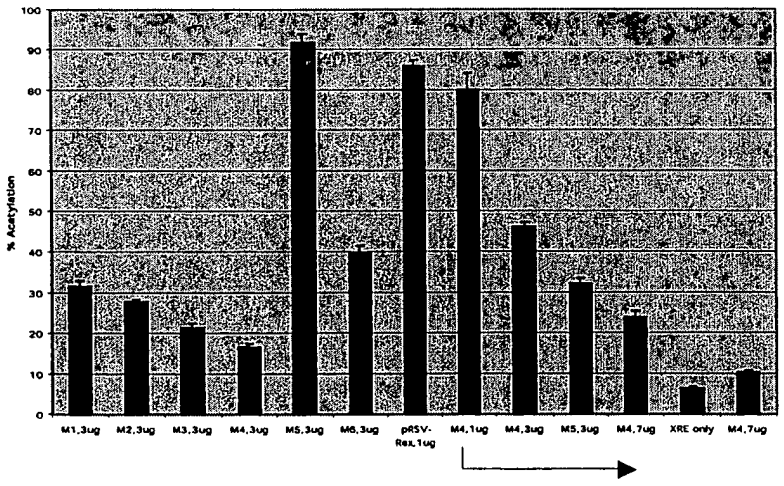


Figure 19

1 MPKERRSRRRPQ---PIIRWQVLLVGCPTLYMPARPWFCPMMSPSMPGAPSAGP 51

M7 M8

52 MSDSNSKGSTPRSPARPTVSTGPPMDDLAASMERCSLDCMSPRPAPKGPDDSGSTAPFRP

M9 M10 M6

112 FALSPARFHFPPSSGPPSSPTNANCP 137

M1 AAA

M2 DL

M3 DL

M4 DL

M5 DL

M6 (R85A) : Mutation of BLV NES

Double Mutant : Δ7/M4

Δ2 : M2–M4

Δ3 : M3–M5

Δ7 : M7–M8

Δ8 : M8–M9

Δ9 : M9–M10

Figure 20

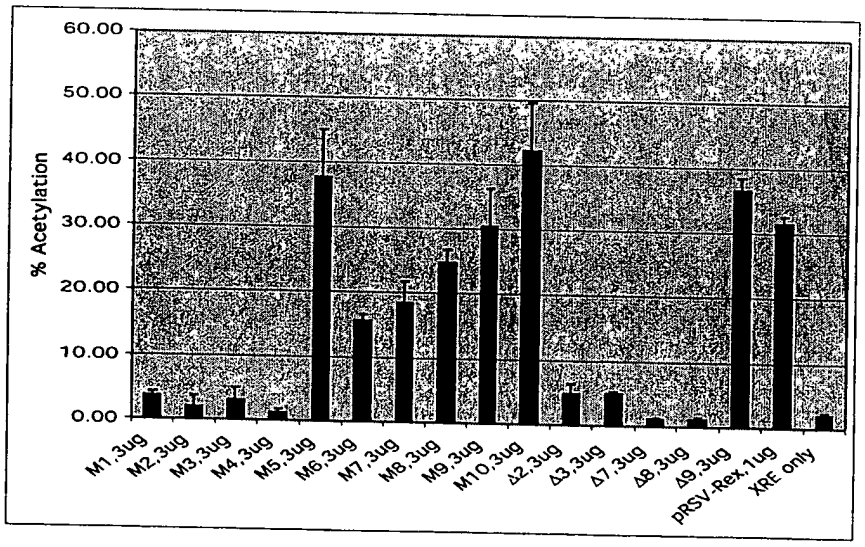


Figure 21

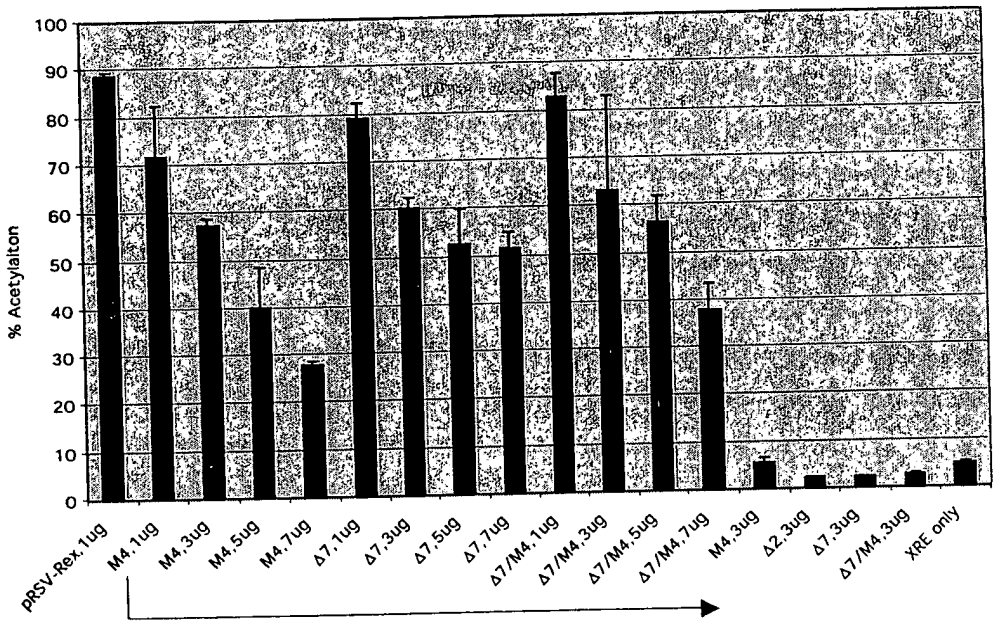

% Acetylalton
100
90
80
70
60
50
40
30
20
10
0
pRSV-Rex.1ug
M4.1ug
M4.3ug
M4.5ug
M4.7ug
Δ7.1ug
Δ7.3ug
Δ7.5ug
Δ7.7ug
Δ7/M4.1ug
Δ7/M4.3ug
Δ7/M4.5ug
Δ7/M4.7ug
M4.3ug
Δ2.3ug
Δ7.3ug
Δ7/M4.3ug
XRE only

Figure 22A

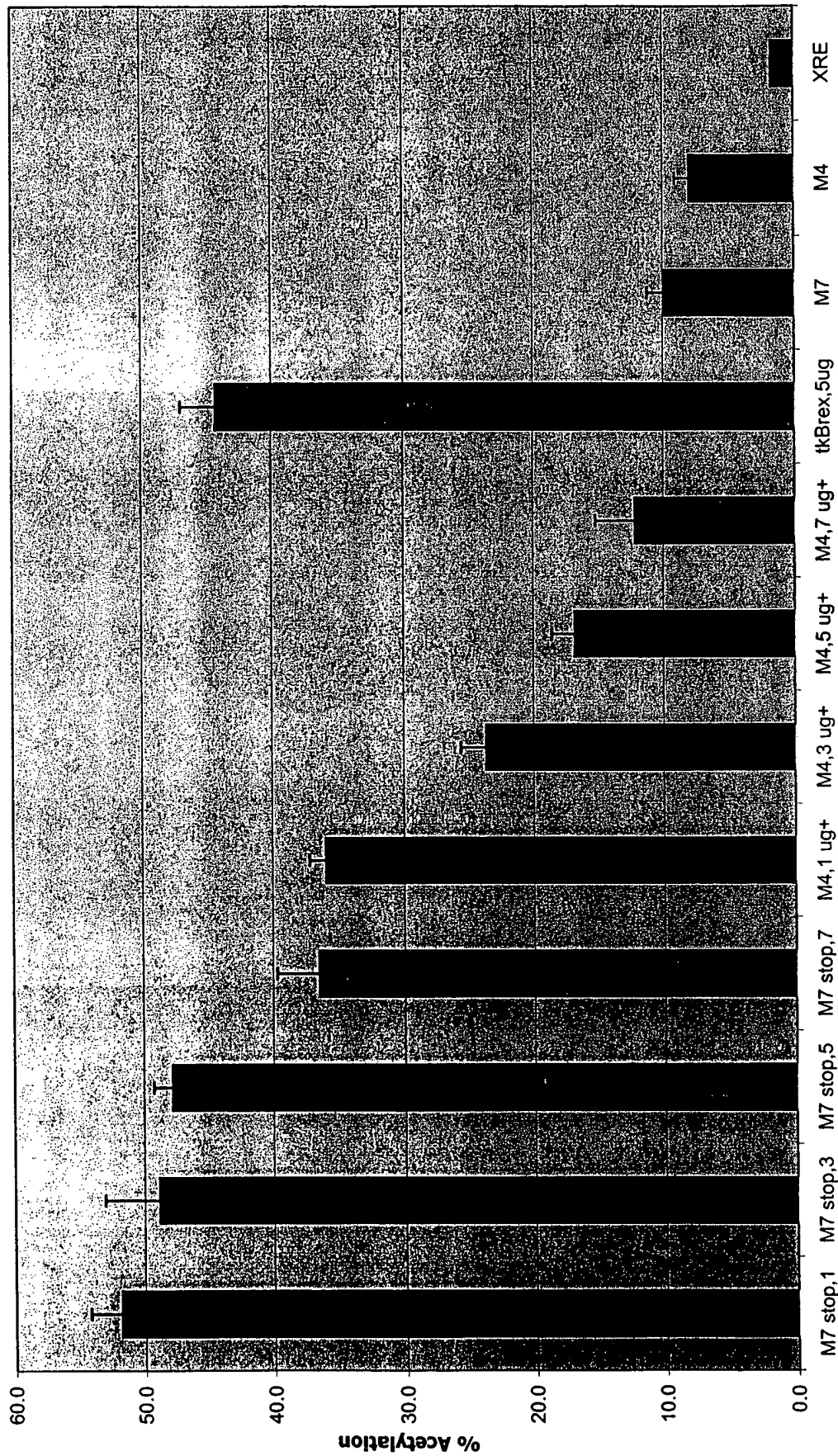

% Acetylation
60.0
50.0
40.0
30.0
20.0
10.0
0.0
M7 stop,1 ug+ tkBrex,5ug
M7 stop,3 ug+ tkBrex,5ug
M7 stop,5 ug+ tkBrex,5ug
M7 stop,7 ug+ tkBrex,5ug
M4,1 ug+ tkBrex,5ug
M4,3 ug+ tkBrex,5ug
M4,5 ug+ tkBrex,5ug
M4,7 ug+ tkBrex,5ug
tkBrex,5ug
M7 stop,7ug
M4
XRE

Figure 2B

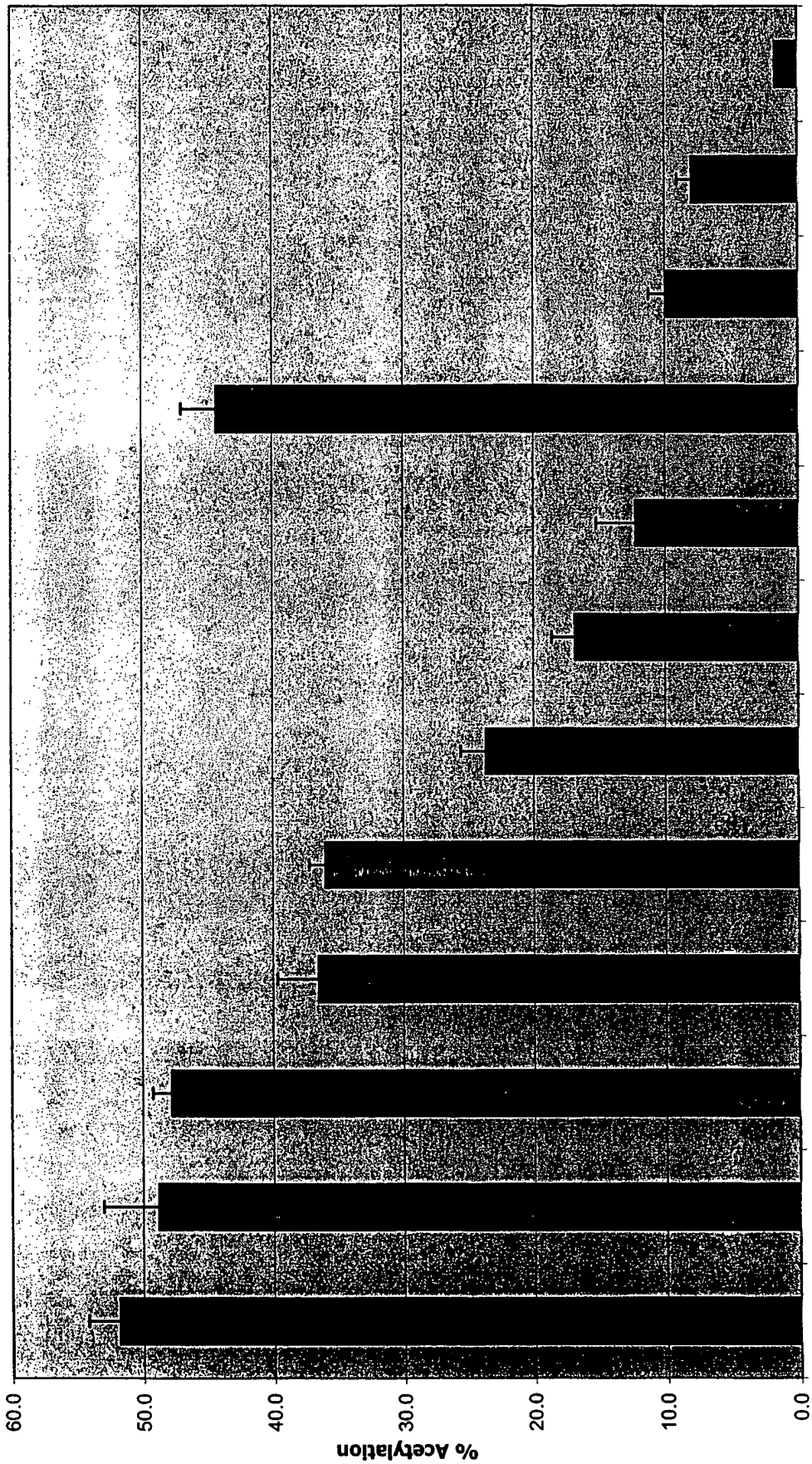

% Acetylation
60.0
50.0
40.0
30.0
20.0
10.0
0.0
M7 stop,1 ug+ tkBrex,5ug
M7 stop,3 ug+ tkBrex,5ug
M7 stop,5 ug+ tkBrex,5ug
M7 stop,7 ug+ tkBrex,5ug
M4,1 ug+ tkBrex,5ug
M4,3 ug+ tkBrex,5ug
M4,5 ug+ tkBrex,5ug
M4,7 ug+ tkBrex,5ug
tkBrex,5ug
M7 stop,7ug
M4
XRE

Figure 22 C

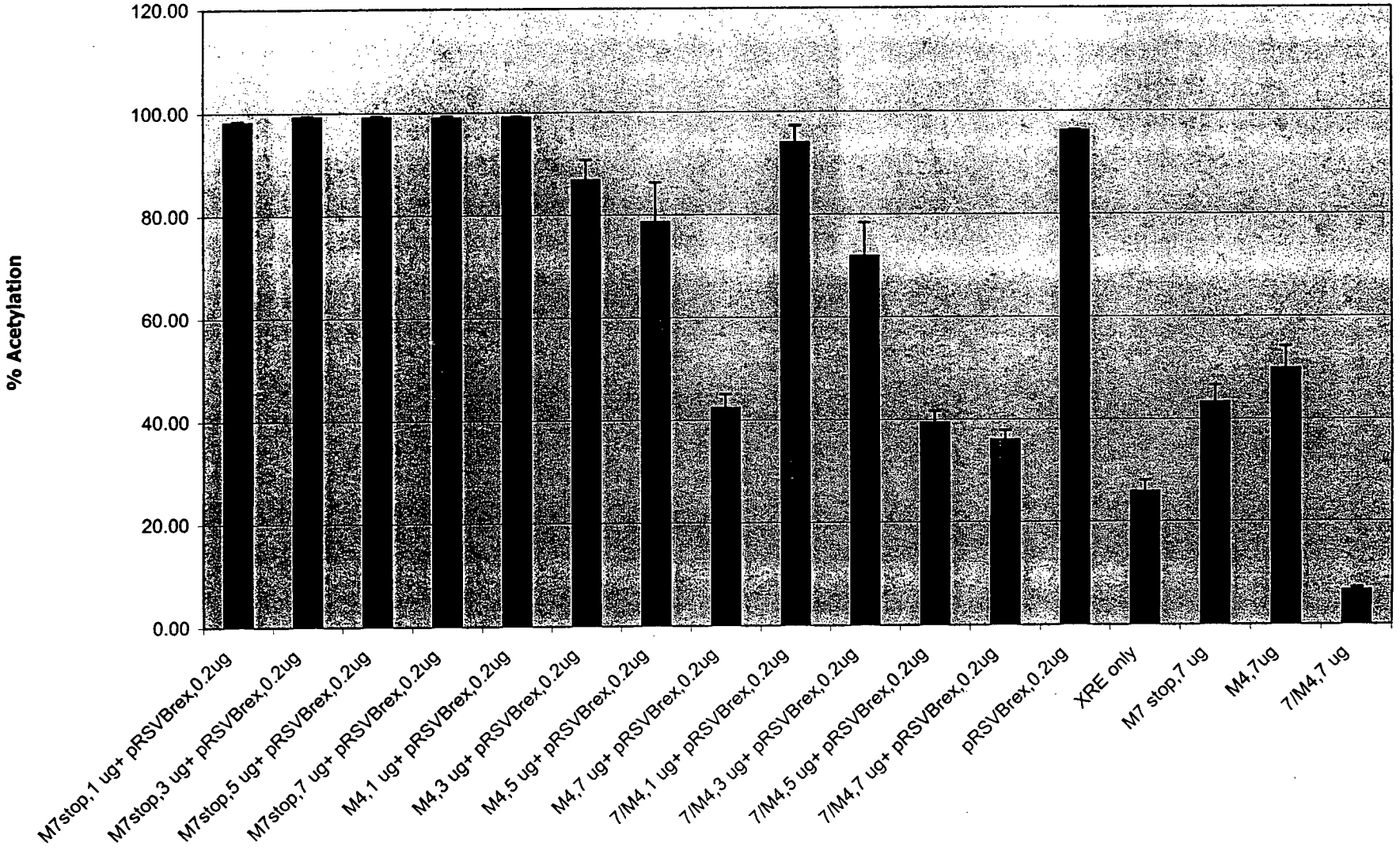

% Acetylation
120.00
100.00
80.00
60.00
40.00
20.00
0.00
M7stop,1 ug+ pRSVBrex,0.2ug
M7stop,3 ug+ pRSVBrex,0.2ug
M7stop,5 ug+ pRSVBrex,0.2ug
M7stop,7 ug+ pRSVBrex,0.2ug
M4,1 ug+ pRSVBrex,0.2ug
M4,3 ug+ pRSVBrex,0.2ug
M4,5 ug+ pRSVBrex,0.2ug
M4,7 ug+ pRSVBrex,0.2ug
7/M4,1 ug+ pRSVBrex,0.2ug
7/M4,3 ug+ pRSVBrex,0.2ug
7/M4,5 ug+ pRSVBrex,0.2ug
7/M4,7 ug+ pRSVBrex,0.2ug
pRSVBrex,0.2ug
XRE only
M7 stop,7 ug
M4,7ug
7/M4,7 ug

Figure 23

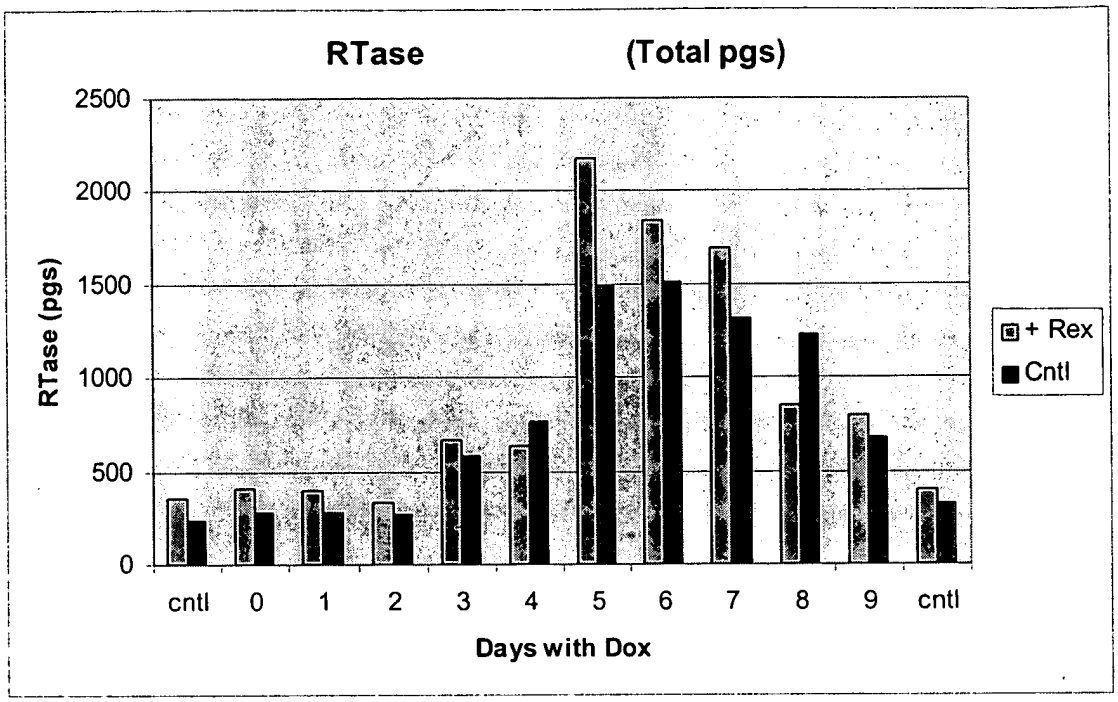

RTase (Total pgs)
2500
2000
1500
1000
500
0
RTase (pgs)
cntl
0
1
2
3
4
5
6
7
8
9
cntl
Days with Dox
+ Rex
Cntl

Figure 24

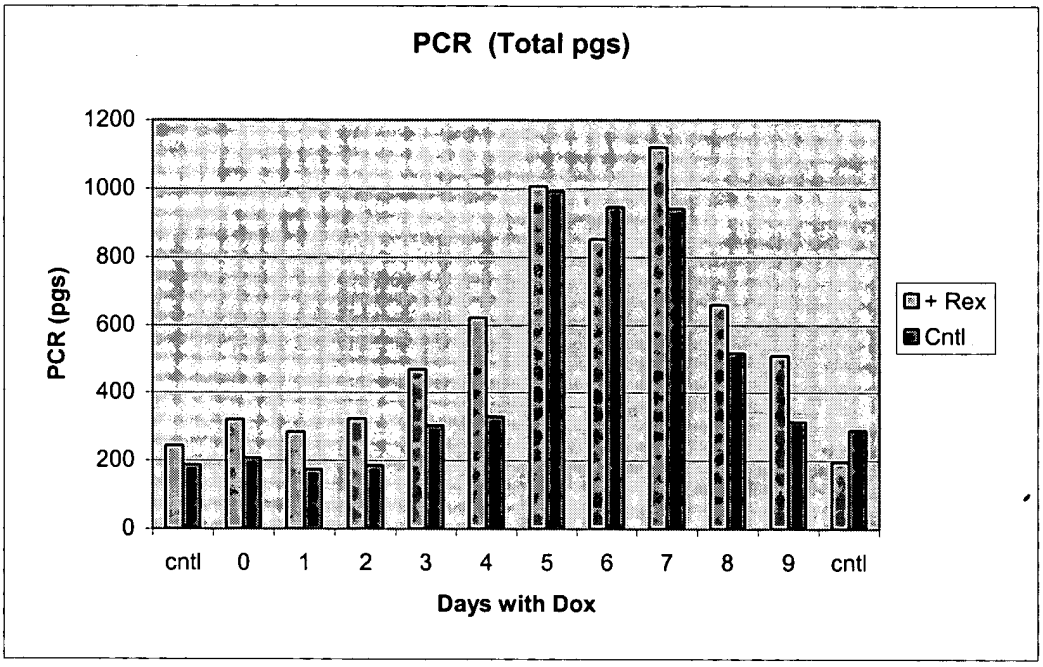

PCR (Total pgs)
PCR (pgs)
1200
1000
800
600
400
200
0
cntl
0
1
2
3
4
5
6
7
8
9
cntl
Days with Dox
+ Rex
Cntl

Figure 25

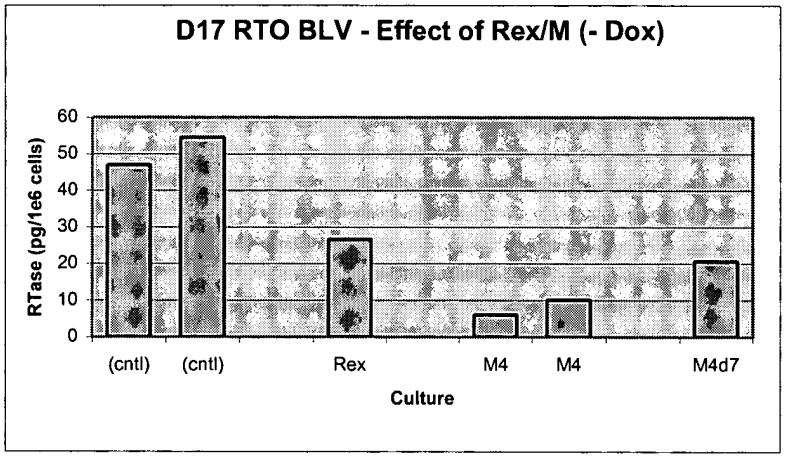

D17 RTO BLV - Effect of Rex/M (- Dox)
RTase (pg/1e6 cells)
60
50
40
30
20
10
0
(cntl)
(cntl)
Rex
M4
M4
M4d7
Culture

Figure 26

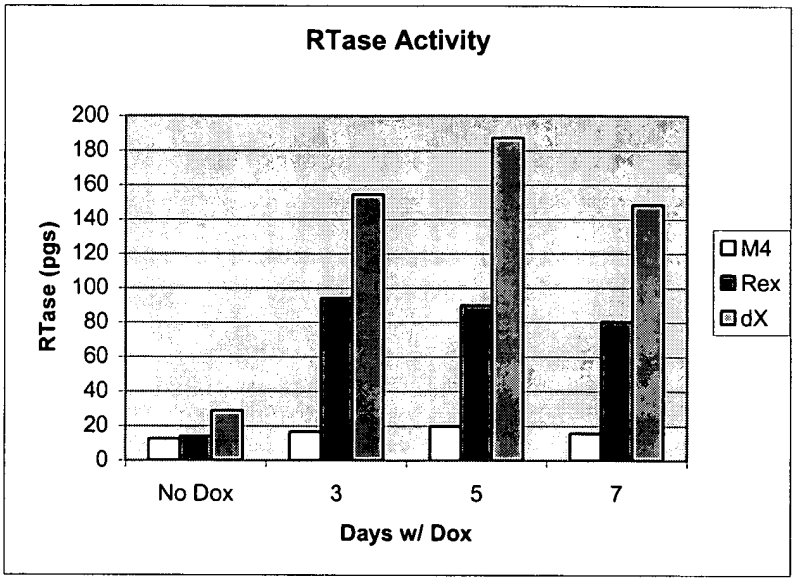

RTase Activity
RTase (pgs)
200
180
160
140
120
100
80
60
40
20
0
No Dox
3
5
7
Days w/ Dox
M4
Rex
dX

Figure 27

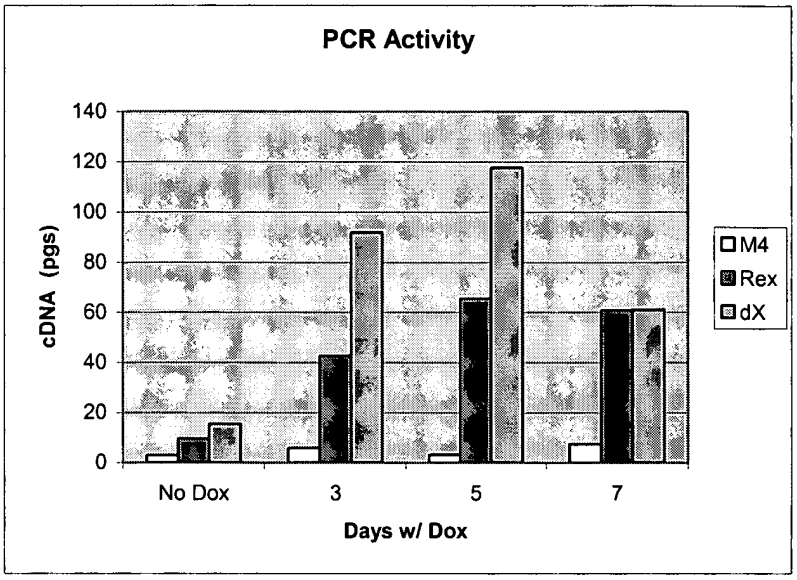

PCR Activity
140
120
100
80
60
40
20
0
cDNA (pgs)
No Dox
3
5
7
Days w/ Dox
M4
Rex
dX

Figure 28

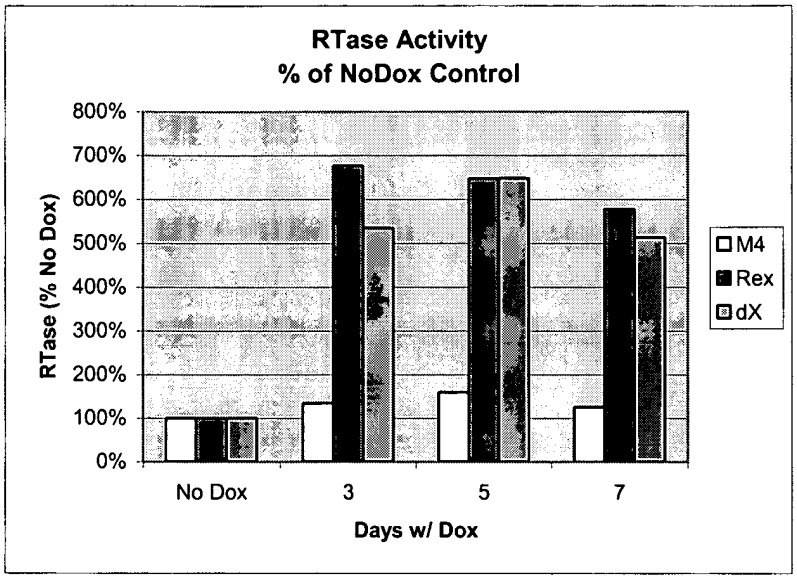

RTase Activity
% of NoDox Control
800%
700%
600%
500%
400%
300%
200%
100%
0%
RTase (% No Dox)
No Dox
3
5
7
Days w/ Dox
M4
Rex
dX

Figure 29

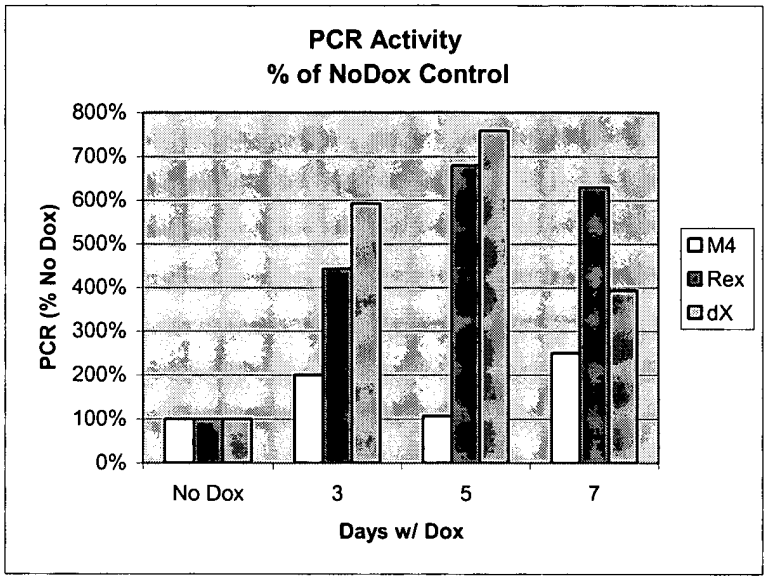
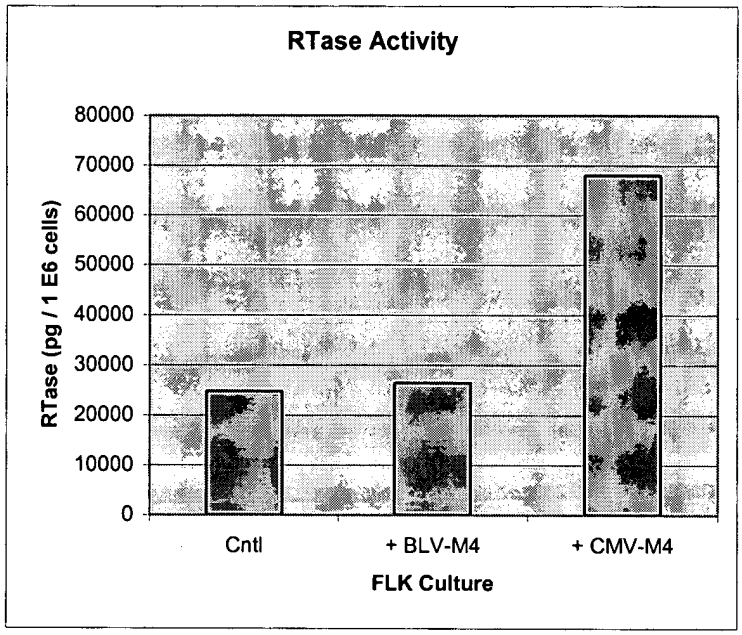

PCR Activity
% of NoDox Control
800%
700%
600%
500%
400%
300%
200%
100%
0%
PCR (% No Dox)
No Dox
3
5
7
Days w/ Dox
M4
Rex
dX

Figure 30


RTase Activity
RTase (pg / 1 E6 cells)
80000
70000
60000
50000
40000
30000
20000
10000
0
Cntl
+ BLV-M4
+ CMV-M4
FLK Culture